White matter neuroregeneration after chemotherapy: stem cell therapy for “chemobrain”

Grant Award Details

White matter neuroregeneration after chemotherapy: stem cell therapy for “chemobrain”

Grant Type: New Faculty Physician Scientist

Grant Number: RN3-06510

Project Objective: To define and capitalize on mechanisms of neuronal instruction of oligodendrogliogenesis to encourage OPC population repair and white matter regeneration following chemotherapy exposure. The initial phase of the project (2.5 years) is dedicated to further validating and optimizing the experimental model systems with which the team will define a therapeutic strategy for chemotherapy-induced OPC population depletion and white matter injury, and to identifying the therapeutically targetable mechanism(s) that underlie the mitogenic effect of active neurons on OPCs.

Investigator:

Name:	Michelle Monje
Institution:	Stanford University
Type:	PI

Disease Focus: Brain Cancer, Cancer, Neurological Disorders, Solid Tumors

Human Stem Cell Use: Adult Stem Cell, Embryonic Stem Cell

Award Value: $2,800,536

Status: Active

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: White matter neuroregeneration after chemotherapy: stem cell therapy for “chemobrain”

Public Abstract:

Chemotherapy for cancer is often life saving, but it also causes a debilitating syndrome of impaired cognition characterized by deficits in attention, concentration, information processing speed, multitasking and memory. As a result, many cancer survivors find themselves unable to return to work or function in their lives as they had before their cancer therapy. These cognitive deficits, colloquially known as "chemobrain" or "chemofog," are long-lasting and sometimes irreversible. For example, breast cancer survivors treated with chemotherapy suffer from cognitive disability even 20 years later.

These cognitive problems occur because chemotherapy damages the neural stem and precursor cells necessary for the health of the brain's infrastructure, called white matter. We have discovered a powerful way to recruit the stem/precursor cells required for white matter repair that depends on an interaction between the electrical cells of the brain, neurons, and these white matter stem/precursor cells. In this project, we will determine the key molecules responsible for the regenerative influence of neurons on these white matter stem cells and will develop that molecule (or molecules) into a drug to treat chemotherapy-induced cognitive dysfunction. If successful, this will result in the first effective treatment for a disease that affects at least a million cancer survivors in California.

Statement of Benefit to California:

Approximately 100,000 Californians are diagnosed with cancer each year, and the majority of these people require chemotherapy. While cancer chemotherapy is often life saving, it also causes a debilitating neurocognitive syndrome characterized by impaired attention, concentration, information processing speed, multitasking and memory. As a result, many cancer survivors find themselves unable to return to work or function in their lives as they had before their cancer therapy. These cognitive deficits, colloquially known as "chemobrain" or "chemofog" are long-lasting; for example, cognitive deficits have been demonstrated in breast cancer survivors treated with chemotherapy even 20 years later. With increasing cancer survival rates, the number of people living with cognitive disability from chemotherapy is growing and includes well over a million Californians. Presently, there is no known therapy for chemotherapy-induced cognitive decline, and physicians can only offer symptomatic treatment with medications such as psychostimulants.

The underlying cause of "chemobrain" is damage to neural stem and precursor cell populations. The proposed project may result in an effective regenerative strategy to restore damaged neural precursor cell populations and ameliorate or cure the cognitive syndrome caused by chemotherapy. The benefit to California in terms of improved quality of life for cancer survivors and restored occupational productivity would be immeasurable.